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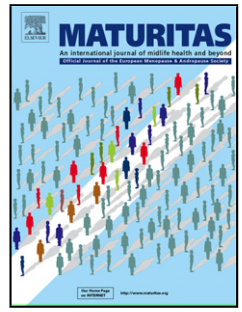

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Exercise Prescription for the Older Population: The Interactions Between Physical Activity, Sedentary Time, and Adequate Nutrition in Maintaining Musculoskeletal Health

Running title: Physical activity, nutrition, and musculoskeletal health in older adults

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Highlights

- The minimum amount of physical activity needed to promote musculoskeletal function for older adults is poorly defined.
- The combination of physical activity and adequate nutrition is critical for maintaining skeletal muscle mass and metabolic health.
- Further research is required to examine the feasibility of breaking up or reducing sedentary time as a strategy to improve muscle anabolic sensitivity and thus maintain musculoskeletal health in older individuals.
- The feasibility of reducing sedentary time to maintain musculoskeletal health in older individuals needs to be explored.
- Physical activity guidelines should be modified to highlight the importance of nutrition combined with resistance-type exercise.

Abstract

Regular physical activity (PA) promotes musculoskeletal health in older adults. However, the majority of older individuals do not meet current PA guidelines and are also highly sedentary. Emerging evidence indicates that large amounts of sedentary time accelerate the loss of skeletal muscle mass (i.e., sarcopenia) and physical function with advancing age. However, current PA recommendations for sedentary time are non-specific (i.e., keep sedentary time to a minimum). Research indicates that physical inactivity and large amounts of sedentary time accelerate sarcopenic muscle loss by inducing skeletal muscle 'anabolic resistance'. These findings suggest a critical interaction between engaging in 'sufficient' levels of PA, minimising sedentary time, and consuming 'adequate' nutrition to promote optimal musculoskeletal health in older adults. However, current PA recommendations do not take into account the important role that nutrition plays in ensuring older adults can maximise the benefits from the PA in which they engage. The aim of this narrative review is: 1) to briefly summarise the evidence used to inform current public health recommendations for PA and sedentary time in older adults; and 2) to discuss the presence of 'anabolic resistance' in older adults, highlighting the importance of regular PA and minimising sedentary behaviour. It is imperative that the synergy between PA, minimising sedentary behaviour and adequate nutrition is integrated into future PA guidelines to promote optimal musculoskeletal health and metabolic responses in the growing ageing population.

KEYWORDS: Physical activity; exercise; inactivity; sedentary; musculoskeletal function; anabolic resistance.

1. Introduction

Benefits of physical activity (PA) for older adults, particularly in the forms of resistance (e.g., muscular contraction using free-weights) and endurance (e.g., running or cycling) types of exercise are widely recognised. Regular PA has been shown to improve physical function and quality of life [1, 2], prevent sarcopenia, frailty and decrease the risk for cognitive decline [3-5], reduce the risks for obesity, coronary heart disease, and type 2 diabetes [6] and is associated with lower rates of all-cause mortality and diagnosis of new diseases [7].

PA guidelines recommend that older adults engage in a minimum of 150 minutes per week of moderate-to-vigorous intensity PA (MVPA) accumulated in bouts of at least 10 minutes, in addition to some resistance and flexibility exercises at least two days per week to maintain or improve strength and balance [8-11]. MVPA is typically defined as any form of PA with a metabolic equivalent (MET) of ≥3 METs. Studies that have objectively measured MVPA in community-dwelling older adults indicate that a very small percentage (<5%) of this population meet the current guidelines [12-16], suggesting that these recommendations may not be realistic or attainable for the majority of older adults. For an in-depth overview of accelerometer-derived physical activity levels in older adults, interested readers are referred to a recent systematic review conducted by Sun and colleagues [16].

In addition to low levels of engagement in PA, sedentary behaviour is highly prevalent in older adults, with objective measures indicating that older adults may spend up to 85% of their waking hours being sedentary [12, 13, 17, 18]. Although emerging cross-sectional evidence suggests that increased time spent sedentary is a risk factor for development of chronic diseases, skeletal muscle loss (i.e., sarcopenia), functional disability, and premature mortality independent of physical activity [19-22], the lack of evidence identifying the specific amount of time spent sedentary that increases one’s risks for diseases and functional disability has resulted in current recommendations for sedentary time being non-specific (i.e., keep sedentary time to a minimum) [9]. It has been argued that it may be easier to intervene to decrease sedentary time within older adults than increase PA to recommended levels, and emerging cross-sectional and experimental evidence highlights the beneficial effect that breaking up prolonged sedentary time can exert on both physical function and metabolic health [23, 24].

Recent evidence suggests the presence of 'anabolic resistance' in older adults, which has been proposed as an important underlying mechanism in the progression of sarcopenia [25, 26]. 'Anabolic resistance' refers to the dysregulation of the muscle protein synthetic response to anabolic stimuli (i.e., exercise and/or protein/amino acid-based nutrition). This research suggests a critical interaction between 'sufficient' levels of exercise and 'adequate' nutrition that promotes optimal physical function and metabolic health in older adults. However, current PA recommendations do not take into account the important role that nutrition plays in ensuring older adults can maximise the benefits from the exercise in which they engage.

The aims of this narrative review are to: i) briefly summarise the evidence used to inform current public health recommendations for PA and sedentary time in older adults; ii) examine what is currently known about the beneficial effects of PA and reduced sedentary time on musculoskeletal health in older adults; iii) discuss the presence of 'anabolic resistance' in older adults, highlighting the interactions between PA and nutritional intake in optimising functional and metabolic responses in older adults; and iv) re-examine the current recommendations for PA and sedentary time in light of the evidence presented.

2. Methods

A narrative review was conducted, drawing upon the international English-language literature published up to April 2016, using the Ovid MEDLINE (1946 to April 2016) and EMBASE

(1974 to 10th April 2016) databases. Search terms were: “human/humans,” “old,” “elder,” “physical activity,” “exercise,” “physical activity recommendations,” “physical activity guidelines,” “physical inactivity,” “sedentary behaviour,” “sedentary time,” “musculoskeletal,” “health,” “protein synthesis,” “muscle protein synthesis,” “fractional synthetic rate,” “muscle protein accrual,” “protein balance,” “amino acid,” “essential amino acid,” “dietary protein,” “muscle disuse,” and “anabolic resistance.” Boolean operators “and” and “or” were used to combine search terms. Additional studies were identified through the reference lists of articles (e.g. reviews) from relevant fields of study.

3. Evidence Informing Current Guidelines on Physical Activity and Sedentary Behaviour

There is consistently strong evidence indicating a positive association between increased PA and reduced risks for all-cause mortality, cardiovascular disease (CVD), type 2 diabetes, metabolic syndrome, and falls [8, 9]. The cross-sectional evidence linking increased sedentary time with elevated risk for all-cause mortality, CVD and metabolic diseases is relatively recent [19-21] and not without controversy [27]. Although the health benefits of regular PA are well documented, the exact amount and type of PA needed to achieve the greatest benefits in older adults is not clear, and how this may differ for various diseases and functional conditions is not known. In addition, most of the evidence used to develop current PA guidelines from various countries [8-11] is based on self-reported data from young and middle-aged adults, is predominantly observational in nature, and as such is subject to limitations such as self-report bias, poor generalizability to older adults, and lack of precision regarding the minimum amount of PA needed to optimise musculoskeletal health and function.

It is important to recognise that older adults are not functionally, cognitively or metabolically homogeneous, and as such the levels of PA needed to optimise musculoskeletal health and function will vary widely, which draws into question the usefulness of a one-size-fits-all set of recommendations for this growing segment of the global population. Current PA guidelines recognise this diversity across the older population, and have included caveats such as: 1) being as physically active as possible when one cannot meet recommendations due to chronic conditions; 2) determining the appropriate level of effort for PA relative to one's level of fitness and functional capacity; and 3) for those with chronic conditions, understanding how their condition may affect their ability to do PA safely [8, 9]. However, the predominant message communicated to older adults via public health and clinical settings is that they should be striving to engage in a minimum of 150 minutes per day of MVPA and engage in strength exercises twice per week.

4. Physical Activity, Sedentary Time, and Musculoskeletal Health

Evidence generated from experimental studies at the whole-body and cellular level indicate that regular participation in MVPA is fundamental to the preservation of skeletal muscle mass, strength, and physical function with advancing age [28, 29]. Though some loss of muscle mass and strength (i.e., sarcopenia) in later life may be inevitable, regular PA provides an effective means of slowing the progression of this debilitating condition [28]. The skeletal muscle adaptive response to regular participation in PA is highly variable across all ages [30, 31]. Nevertheless, evidence suggests that all older adults maintain a relatively high level of muscle plasticity, allowing skeletal muscle tissue to adapt to prolonged resistance-type exercise training [30, 31]. This highlights the importance of staying physically active throughout the lifespan.

As stated in the introduction, research has now started to focus on the negative health consequences of high sedentariness independent of a person's level of physical inactivity (i.e., the failure to meet current physical activity guidelines). The terms "sedentary" and "physically inactive" are often used interchangeably, however, researchers within the field recently proposed the act of being sedentary as 'any waking behaviour characterized by an energy expenditure ≤1.5 METs while in a sitting or reclining posture'[32]. In contrast, the term "physically inactive" should be reserved for those individuals who fail to perform sufficient amounts of MVPA to meet current recommendations [32]. Applying these definitions, it is apparent that an individual can be sufficiently active yet highly sedentary (e.g., a recreational exerciser who meets PA recommendations whilst also having a highly sedentary job). Similarly, an individual can be physically inactive and fail to meet PA recommendations, yet also partake in minimal sedentary behaviour.

Older adults may spend the majority of their waking hours being sedentary, and emerging research indicates that engaging in sedentary behaviours for prolonged periods (e.g., watching television) negatively impacts skeletal muscle mass and functional capacity in older adults, irrespective of one's level of MVPA [22]. As such, it has been advocated that physical inactivity and sedentariness should be treated as two distinct risk factors, and be targeted individually in order to achieve optimal musculoskeletal health. Whilst intriguing, much of the current evidence linking sedentary behaviour and musculoskeletal health is of an observational nature, based on cross-sectional data that do not establish a causative link [22, 23]. Moreover, evidence has often been obtained using methodology prone to bias to assess primary outcome measures (e.g., assessment of sedentary time and functional capacity using self-report questionnaires) [22, 33]. As such, our current understanding of the complex interaction between sedentariness and musculoskeletal health in older adults remains poorly defined.

5. Anabolic Resistance in Older Adults

Experimental interventions employing muscle disuse (e.g., bed rest and limb immobilisation) as a model of physical inactivity provide direct physiological evidence that brief and protracted unloading of skeletal muscle results in a loss of muscle mass, strength and physical function in older adults [34, 35]. Importantly, the increasing frequency of brief bouts of muscle disuse often experienced with advancing age (e.g., due to being hospitalised, injured or confined to the home due to adverse weather conditions) has been postulated as a contributing factor to the sarcopenic process [36]. This highlights the importance of regular engagement in PA and minimising time spent sedentary to maintain optimal musculoskeletal health and physical function into older age.

Skeletal muscle is comprised of specific protein sub-fractions (e.g., myofibrillar, mitochondrial and sarcoplasmic) which vary in their responsiveness (i.e., protein remodelling) to different modes of exercise [37, 38]. Skeletal muscle mass is regulated by the net protein balance between muscle protein synthesis and muscle protein breakdown. Skeletal muscle growth occurs when muscle protein synthesis chronically exceeds muscle protein breakdown [39]. The most effective means of accruing skeletal muscle mass is the combined anabolic stimulus of resistance exercise and adequate protein-based nutrition [40, 41]. It is the rise in plasma essential amino acid availability following protein ingestion that drives the postprandial stimulation of muscle protein synthesis [42]. In contrast, the loss of skeletal muscle mass typically observed following muscle disuse, and with advancing age, occurs when muscle protein breakdown exceeds muscle protein synthesis. Basal, postabsorptive rates of muscle protein synthesis and muscle protein breakdown appear to be similar between young and older individuals and thus are unlikely to explain the loss of skeletal muscle mass observed with advancing age [43, 44]. Instead, it appears that the muscle protein synthetic response to normally robust anabolic stimuli (i.e., exercise and amino acid/protein-based nutrition) is impaired in older adults [25, 26]. It is this 'anabolic resistance' that is thought to underpin the loss of skeletal muscle mass with ageing.

However, it has been proposed that muscle anabolic resistance may be a consequence of declining PA levels and increasing levels of sedentary time typically seen in the older population as opposed to ageing *per se* (Figure 1) [45]. Strong experimental evidence to support this supposition can be taken from findings that demonstrate muscle disuse and a reduction in daily steps (a model that closely resembles high levels of sedentary time) diminish the ability of skeletal muscle to mount a robust anabolic response to protein-based nutrition in older adults [35, 46]. Indeed, just five days of muscle disuse impairs the ability of skeletal muscle tissue to utilise dietary protein-derived amino acids for *de novo* muscle protein synthesis in young adults [47]. In contrast, resistance-type exercise sensitises skeletal muscle tissue to the anabolic properties of protein-based nutrition, improving the capacity of skeletal muscle tissue to utilise dietary protein-derived amino acids for *de novo* muscle protein synthesis in young and older adults [48]. Collectively, these findings highlight the synergy between adequate levels of PA and dietary protein intake in maintaining musculoskeletal health and function in older adults. This synergy between PA and diet should be integrated into future PA guidelines and applied in clinical and community-based settings to prevent sarcopenia and functional dependency.

Exercise has been shown to increase the sensitivity of senescent muscle to the anabolic properties of protein-based nutrition [48]. In line with these findings, resistance-type exercise and neuromuscular electrical stimulation have been shown to be effective in preserving muscle anabolic sensitivity and, as such, skeletal muscle mass [49-51]. What remains to be assessed is whether a reduction in sedentary time or the discontinuation of prolonged periods of sitting are also of sufficient magnitude to improve the sensitivity of skeletal muscle tissue to the anabolic properties of protein-based nutrition. Thus, research is warranted to assess whether breaking up prolonged bouts of sedentary time (with activities that are of an insufficient intensity and/or duration to meet current PA guidelines) can also exert a similar protective effect upon skeletal muscle mass and physical function. Cross-sectional data indicate a positive correlation between breaks in sedentary time and physical function after adjusting for MVPA levels [23]. Promising findings suggest that low-intensity walking can enhance the muscle protein synthetic response to protein-based nutrition in older adults [52]. Furthermore, breaking up prolonged sitting with brief two-minute bouts of walking every twenty minutes has been shown to improve postprandial glycaemic control in older adults, presumably through enhanced peripheral glucose uptake as a result of repeated skeletal muscle contractions [24].

Taken together, these findings suggest that relatively low-intensity skeletal muscle contractions (e.g., walking) may be sufficient to sensitise senescent muscle to the anabolic properties of subsequent food intake. Interestingly, the beneficial effect observed when breaking up sitting with walking is not replicated when prolonged sitting is fragmented with standing, and thus it is possible that more than simple muscle contraction is needed to achieve this nutrient sensitising effect [53]. Coupling the paucity of available evidence with the high prevalence of sedentariness in older adults, it is imperative that future interventions should focus on determining the efficacy of breaking up prolonged bouts of sedentary time with a sufficient amount of movement as a strategy to preserve skeletal muscle anabolic sensitivity, muscle mass and physical function in this population.

6. Conclusion

The benefits of PA in optimising musculoskeletal function and metabolic health are well established, but the minimum amount of PA needed for older adults remains poorly defined. The coupling of PA (i.e., resistance-type exercise) and adequate nutrition (i.e., sufficient intake of essential amino acids/protein sources) is critical for preserving muscle anabolic sensitivity and thus maintaining skeletal muscle mass and metabolic health with advancing age [48]. As such, we strongly recommend that guidelines for PA in older adults are modified to incorporate and highlight the importance of adequate nutrition combined with resistance-type exercise training to promote musculoskeletal health in this segment of the population.

Although we recognise the benefits that can be derived for older adults when they meet current MVPA guidelines, these guidelines may not be attainable for the majority of older adults. Based on emerging evidence from a limited number of published studies, it appears that breaking up sedentary time regularly with a sufficient level of movement that goes beyond a simple muscular contraction (e.g., walking as opposed to standing) may be sufficient to preserve skeletal muscle anabolic sensitivity, muscle mass, and physical function in older adults [23, 52]. Therefore, future research is required to examine the feasibility of breaking up or reducing sedentary time as a strategy to improve muscle anabolic sensitivity and thus maintain musculoskeletal health in older individuals. It is our hope that findings from research in this area will contribute to the formulation of specific public health guidelines designed to reduce time spent in sedentary behaviours, and thus preserve musculoskeletal health and physical function in this rapidly growing segment of the global population.

Contributors

BJS and JLT designed and drafted the manuscript.

GW and LJCvL conducted critical revisions of the manuscript.

Final approval of the manuscript was given by all authors.

Conflict of interest

None declared.

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Provenance and peer review

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Ethical Approval

Not applicable as this is a narrative review.

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Figure Captions

Figure 1. Interplay between Physical Activity, Sedentary Behaviour and Muscle Anabolic Resistance: Advancing age typically leads to a decline in physical activity levels and an increase in sedentary time. This combination of physical inactivity and high levels of sedentary behaviour results in a diminished muscle protein synthetic response to protein/amino acid based nutrition (i.e., muscle anabolic resistance). It is this reduction in muscle anabolic sensitivity that likely contributes to the loss of muscle mass and physical function (i.e., sarcopenia) typically seen with ageing. This loss of muscle mass and physical function may promote additional reductions in physical activity and increases in sedentary behaviour, leading to further muscle anabolic resistance and ultimately accelerated declines in musculoskeletal health. Strategies that can effectively increase physical activity levels and/or limit sedentary behaviour are likely to improve muscle anabolic sensitivity, thereby slowing the progression of sarcopenic muscle loss and functional dependency in the ageing population.